Appl. No.: 09/889,321

REMARKS

Claims 1-19 are pending. Claims 13-19 are withdrawn from consideration. Claims 1-12 are rejected. Amendment has been made to claim 9solely to overcome the indefiniteness rejection. No new matter has been added. Entry of the amendment is requested to reduce the issues for appeal. Reconsideration is requested.

Rejection under 35 USC §112, second paragraph

Claim 9 was rejected under 35 USC § 112, second paragraph, as being indefinite. The claim has been amended in accordance with the Examiner's helpful suggestion. Reconsideration and withdrawal of the rejection are respectfully requested.

Rejection under 35 USC §103

Claims 1-12 were rejected under 35 USC §103(a) as being unpatentable over Ilan et al. in view of DeMatteo et al and further in view of Bakker et al. This rejection is traversed for the following reasons.

The examiner asserts that 'the combined teachings of Ilan et al., DeMatteo et al., and Bakker et al.' render the instant invention obvious. However, there is no description or suggestion in any of the cited references, Ilan et al., DeMatteo et al., and Bakker et al., about the basic technical feature of the present invention, that is, "to acquire natural immunological tolerance with the use of 'immature T lymphocyte." Therefore, it is obvious that the present invention is not taught by any combination of the cited references, Ilan et al., DeMatteo et al., and Bakker et al. Because there is no description of the feature in any of the cited references, no combination of the cited references can render the technical feature of the present invention obvious.

The examiner has cited Ilan et al., and stated: "Ilan et al. was cited for establishing that cells containing and expressing foreign DNA can be used to induce tolerance against the foreign gene by directly administering the cells to the thymus," and exemplified the disclosure of Ilan et al., "cells containing and expressing foreign DNA are directly administered to the thymus," as a

Appl. No.: 09/889,321

disclosure which teaches the present invention.

However, this conclusion is not correct. Briefly, in the present invention, "acquired immunological tolerance can be induced by using the above mechanism of acquiring immunological tolerance in the process of differentiation of the 'immature T lymphocytes' in thymus, by integrating genes expressing antigen into the 'immature T lymphocytes' and introducing the 'immature T lymphocytes' into thymus." By a method such as Ilan's, wherein only "cells containing and expressing foreign DNA" are administered, and "immature T lymphocytes" are not used, the advantage of the present invention, that is, that "acquired immunological tolerance can be induced by using the above mechanism of acquiring immunological tolerance in the process of differentiation of the 'immature T lymphocytes' in thymus," cannot be obtained. As stated above, Ilan et al. does not disclose "inducing acquired immunological tolerance by introducing 'immature' cells," therefore, even if this cited reference and the description of other cited references such as Bakker et al. are combined, the present invention is not taught by the combination.

The examiner has stated: "Bakker et al. was then cited to further supplement Ilan et al. and DeMatteo et al. by teaching methods of infecting fetal T lymphocytes with recombinant adenovirus in vitro in fetal thymic organ culture," and further stated: "motivation to substitute fetal T lymphocytes for hepatocytes in the methods of Ilan et al. is provided by all of Ilan et al., DeMatteo et al., and Bakker et al." This conclusion of the examiner is also improper. In this regard, the examiner has stated that "The teachings of Ilan et al. were supplemented with the teachings of DeMatteo et al., and Bakker et al. Specifically, DeMatteo et al. was cited to supplement the teaching of Ilan et al., by teaching that adenovirus is capable of infecting fetal T lymphocytes in fetal thymus and further that the transduced fetal T lymphocytes induce tolerance (DeMatteo et al., page 5330, abstract, and Figure 1)." However, as DeMatteo et al. does not describe "fetal thymus," this conclusion of the examiner is not correct.

Appl. No.: 09/889,321

The applicant rebuts the examiner's statement, "motivation to substitute fetal T lymphocytes for hepatocytes in the methods of Ilan et al. is provided by Bakker et al.," as follows.

As described in the cited reference, Bakker et al. discloses use of a novel technique combining "adenovirus-mediated gene transfer" and "fetal thymic organ culture (FTOC)" "to determine at which stage of fetal thymic development NF-κB is critical" (for example, see abstract, page 3456, 10th to 7th lines from the bottom). In other words, this reference discloses that adenovirus-mediated introduction is employed when a gene is introduced into "fetal thymic organ culture", and this gene introduction by Bakker et al. is the same method as that of Ilan et al., wherein adenoviral vectors are used to introduce foreign DNA into thymus. Therefore, even when Ilan et al. and Bakker et al. are combined, the combination only teaches that adenoviral vectors are used to introduce foreign DNA into thymus. The examiner has stated: "motivation to substitute fetal T lymphocytes for hepatocytes" is provided by Bakker et al. However, as Bakker et al. does not disclose that gene-transferred cells are further used for gene transfer, the examiner's position is groundless. Further, as previously mentioned, Ilan et al. and Bakker et al. do not disclose "acquired immunological tolerance can be induced by introducing 'immature' cells". Therefore, it is clear that even if the cited references Ilan et al. and Bakker et al. are combined, the present invention is not taught by the combination.

As specifically described above, it is respectfully submitted that the position of the examiner, who has stated: "the office has established that the combined teachings of Ilan et al., DeMatteo et al., and Bakker et al. render the instant invention obvious", is groundless once the disclosures of the cited references are correctly understood. Reconsideration and withdrawal of the rejection are respectfully requested.

As stated above, even when the disclosures of Bakker et al., DeMatteo et al., and Ilan et al., are considered together, the present invention is not taught by the combination. Therefore, it is respectfully requested that the rejection of claims 1-12 under 35 U.S.C.103 (a) as being

Appl. No.: 09/889,321

unpatentable over Ilan et al. (1996), in view of DeMatteo et al. (1997), and further in view of Bakker et al. (1999) be withdrawn.

All rejections having been addressed, it is respectfully submitted that the application is in order for allowance, and Notice to that effect is respectfully requested.

Respectfully submitted,

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